

ORIGINAL CONTRIBUTIONS

Relation between Exposure to Environmental Tobacco Smoke and Lung Cancer in Lifetime Nonsmokers

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To assess the relation between exposure to environmental tobacco smoke throughout life and lung cancer in lifetime nonsmokers, the authors conducted in-person interviews with 41 male and 69 female never-smoking lung cancer cases and 117 male and 187 female never-smoking controls between 1983 and 1990 as part of a hospital-based case-control study of tobacco-related cancers. Cases had newly diagnosed, histologically confirmed primary carcinoma of the lung. Controls were matched to cases on age (± 5 years), sex, race, hospital, and year of interview. Subjects were asked about environmental tobacco smoke exposure in childhood, in adulthood at home, in different jobs, and in transportation and social situations. In addition to amount smoked by family members in the subject's presence, subjects were asked to rate the intensity of each exposure, and married subjects were asked whether their spouse smoked in the bedroom. Several independent indicators of exposure to smoking by spouses were strongly correlated, thereby increasing confidence in the classification of exposure status. The reproducibility of environmental tobacco smoke variables was good for qualitative measures (yes/no), in agreement with previous studies. There were few associations of exposure in specific settings with lung cancer. Males whose wives smoked had an odds ratio of 1.60 (95% confidence interval (CI) 0.67–3.82) and females whose husbands smoked had an odds ratio of 1.08 (95% CI 0.60–1.94). While this study had limited sample size, the pattern of odds ratios shows little indication of an association of environmental tobacco smoke with lung cancer in nonsmokers. *Am J Epidemiol* 1995; 142:141–8.

case-control studies; lung neoplasms; smoking; tobacco smoke pollution

Over 30 epidemiologic studies have examined the relation between exposure to environmental tobacco smoke and lung cancer in lifetime nonsmokers. These studies have been summarized and subjected to pooled analysis in a recent US Environmental Protection Agency report (1). The most common measure of exposure was marriage to a smoker versus marriage to a nonsmoker and the amount smoked by the spouse. The overall relative risk among women whose husbands smoked, relative to women whose husbands did not smoke, across different studies carried out in the United States, was 1.19 (90 percent confidence inter-

val 1.04–1.35) (1). Due to the lack of a biomarker of long-term exposure and consequent reliance on self-reported exposure histories, assessment of exposure throughout life is a central methodological issue in epidemiologic studies of environmental tobacco smoke and chronic disease. Other methodological issues include: misclassification of current or past smokers as never smokers; the availability of histologic confirmation; data collection methods (use of surrogates; telephone/mailed interviews); and potential confounding.

The present study was undertaken to investigate the association of environmental tobacco smoke with lung cancer in nonsmokers in greater depth, following an analysis of a limited set of questions asked during 1978–1980 (2). Detailed information regarding exposure at different periods of life was obtained in order to evaluate exposure from different sources as well as to examine the effect of cumulative exposure in childhood and adulthood. All interviews were conducted with the study subjects themselves. In addition,

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Abbreviations: CI, confidence interval; OR, odds ratio.

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several independent indicators of exposure status were used to increase the validity of exposure assessment.

MATERIALS AND METHODS

A case-control study of environmental tobacco smoke and other risk factors for lung cancer in lifetime nonsmokers was carried out in six hospitals in four cities (New York City, New York; Chicago, Illinois; Detroit, Michigan; and Philadelphia, Pennsylvania) between 1983 and 1990. This study was part of a long-standing case-control study of tobacco-related cancers, which has been described previously (3). In the substudy of lifetime nonsmokers, newly diagnosed, histologically confirmed cases of primary cancer of the lung were ascertained in collaborating hospitals. For each case who was enrolled, up to three control patients who were lifetime nonsmokers matched on age (± 5 years), sex, race, hospital, and date of interview (within 2 months) were enrolled. Controls were patients who were admitted with diagnoses thought not to be associated with tobacco use, including: other cancers (stomach/intestine [22 percent in males, 19 percent in females], breast [1 percent in males, 16 percent in females], prostate [3 percent in males], gynecologic [12 percent in females], lymphatic and hematopoietic [9 percent, 4 percent], skin [4 percent, 2 percent], bone and connective tissue [12 percent, 0 percent], and other cancers [15 percent, 8 percent]), as well as non-cancer diagnoses (orthopedic problems [9 percent, 8 percent], benign prostatic hypertrophy [4 percent in males], genitourinary [1 percent, 4 percent], injury [2 percent, 5 percent], digestive tract [2 percent, 9 percent], other [16 percent, 13 percent]). The age range of subjects was 20–80 years.

All subjects were interviewed in person in the hospital by trained interviewers who administered a questionnaire covering demographics, alcohol intake, occupation and occupational exposures, height and weight, and a detailed history of exposure to environmental tobacco smoke. The latter included items on exposure: in childhood from each household member who smoked (who it was; type of tobacco product smoked; years X smoked in your presence; how many hours per day were you exposed to X's smoke; would you describe your exposure to X's smoke as: none, light, moderate, or heavy); in adulthood in the home (for each smoker, number of cigarettes, pipes, or cigars smoked per day in your presence; years exposure started and stopped; number of hours per day of exposure; intensity of exposure; if spouse(s) smokes, does/did he/she smoke in your bedroom); at work (for four jobs that lasted one year or more, hours per week of exposure; years exposure started and stopped; average number of smokers within 10 feet (3.05 m);

intensity). In addition, information was obtained on exposures of at least 1 year in cars and other forms of transportation (hours per week; years) and in social settings (hours per week; years).

Age 21 years was used as the cutoff between childhood/adolescence and adulthood. Codes were provided for roommates to enable coding of exposures in college dormitories and other living arrangements.

Subjects were considered lifetime nonsmokers if they had never consumed as much as 1 cigarette per day for a year, or had smoked fewer than 365 cigarettes over their lifetime. The inclusion of detailed questions regarding the initiation of smoking early in life and amount smoked provides a basis for excluding ex-smokers who quit decades prior to diagnosis but have smoked more than this minimum amount (2). The proportion of never-smokers among all lung cancer cases in the present study (3 percent in males and 8 percent in females) is in good agreement with data from an earlier phase of this study (2) (2 percent in males and 13 percent in females) and with what has been found in other studies that utilized a detailed questionnaire (4).

Exposure to environmental tobacco smoke in different settings and at different periods of life was assessed in terms of ever versus never exposed in a particular setting; number of smokers in the household in childhood and adulthood; and amount smoked by spouse(s). Odds ratios and their 95 percent confidence intervals were computed for levels of exposure in different settings. For continuous variables, means and standard deviations were compared for cases and controls. Tertiles of smoker-years in childhood and adulthood were used to categorize subjects into no/low exposure, moderate exposure, and heavy exposure.

Unconditional logistic regression was used to estimate the effect of exposure with adjustment for covariates, including age, education, and type of hospital (cancer center vs. other). Due to the small number of nonwhites, race was not included as a cofactor, but key analyses were repeated restricted to whites. The number of lung cancer cases was not sufficient to permit analysis of individual histologic types.

RESULTS

Cases and controls were generally similar with regard to age and race/ethnicity (due to matching) and other demographic factors (table 1). The mean age at diagnosis was 55.8 years for male cases, 55.2 years for male controls, 61.4 years for female cases, and 61.1 years for female controls. Adenocarcinoma was the predominant histologic type in both male nonsmokers (70.8 percent) and female nonsmokers (59.4 percent). The remaining cell types were distributed as follows:

TABLE 1. Distribution (%) of demographic variables among lifetime nonsmoker lung cancer cases and controls in a US hospital case-control study, 1983–1990

Variable	Males		Females	
	Cases (n = 41)	Controls (n = 117)	Cases (n = 69)	Controls (n = 187)
Age (years)				
<40	12	16	6	7
40–49	20	14	14	11
50–59	22	27	17	17
60–69	32	31	32	39
70–80	15	12	30	27
Years of education				
<12	5	11	19	17
12	24	22	42	37
13–15	22	17	17	25
>15	49	50	22	21
Occupational level				
Professional	44	53	20	24
Skilled	49	29	44	43
Semi-skilled	2	10	9	3
Unskilled	5	8	7	5
Housewife	0	0	20	25
Religion				
Protestant	34	24	33	27
Catholic	41	50	41	49
Jewish	20	21	25	20
Other	5	5	1	4
Marital status				
Single	5	16	3	7
Married	76	78	64	63
Divorced/separated	17	3	4	5
Widowed	2	3	29	25
Race				
White	90	97	89	94
Black	3	3	7	4
Hispanic	0	0	1	1
Other	7	0	3	1

squamous cell carcinoma (males, 7.3 percent; females, 14.5 percent), small cell carcinoma (0 percent, 0 percent), large cell carcinoma (12.2 percent, 13.0 percent), and “other/mixed cell types” (9.8 percent, 13.0 percent).

The majority of subjects reported having been exposed to environmental tobacco smoke for at least 1 year either in childhood, adulthood at home, or in the workplace. Only 12 percent of male cases, 15 percent of male controls, 7 percent of female cases, and 13 percent of female controls reported no exposure in any of these settings for at least 1 year. For all subjects combined, 64.2 percent of exposure in childhood was due to the father alone; 7.2 percent was due to the mother alone; 11.1 percent was due to both parents; and 17.5 percent was due to other household members. The relative contributions from different settings appeared to differ between males and females. Females had a greater frequency of exposure “in adulthood—at

home only” and in other mixed categories that included adulthood exposure in the home.

Environmental tobacco smoke exposure status (yes/no) in different settings and number of smokers in the household in childhood and adulthood generally showed little suggestion of an association with lung cancer (table 2). Exposure in childhood among females (yes/no) was associated with a borderline increased risk (odds ratio (OR) = 1.55, 95 percent confidence interval (CI) 0.95–2.79). The significant associations of 2+ smokers in the household in adulthood with lung cancer in males and of exposure in trains, buses, and other transportation in women are based on very small numbers. Self-reported intensity of exposure from different sources (no effective exposure, light, moderate, or heavy) did not differ between cases and controls (data not shown). Mean values for various measures of exposure at different periods of life showed no significant differences between cases and controls (table 3).

Males whose wives smoked had an odds ratio of 1.60 (95 percent CI 0.67–3.82) (table 4). Men exposed to 1–10 cigarettes per day from their wives had an odds ratio of 0.74 (95 percent CI 0.24–2.23), while men exposed to 11+ cigarettes per day had a significantly elevated odds ratio for lung cancer relative to males with wives who did not smoke (OR = 7.48, 95 percent CI 1.35–41.36), however, this stratum contained only 5 cases and 2 controls. Women who had a husband who smoked had an odds ratio of 1.08 (95 percent CI 0.60–1.94), with women who reported that their husband smoked 1–10 cigarettes per day having an odds ratio of 0.82 (95 percent CI 0.42–1.61) and those who reported husbands who smoked 11+ cigarettes per day having an odds ratio of 1.06 (95 percent CI 0.49–2.30). Among males, the odds ratio for having a spouse who smoked in the bedroom was elevated but not statistically significant relative to 1) having a spouse who smoked but not in the bedroom and 2) to all other spouses (those who smoked but not in the bedroom and nonsmokers combined). Among females, the odds ratios for having a spouse who smoked in the bedroom relative to either referent group were close to 1.0.

Consistent with the elevated odds ratio for females who reported exposure in childhood, the highest tertile of smoker-years in childhood was statistically significant in females (OR = 2.19, 95 percent CI 1.06–4.50) and the linear trend was significant ($p = 0.02$) (table 5). No association was seen for smoker-years in childhood or adulthood or of job-years in males, or of smoker-years in adulthood or job-years in females (table 5).

TABLE 2. Association of environmental tobacco smoke exposure in different settings with lung cancer in lifetime nonsmokers in a US hospital case-control study, 1983–1990

Variable	Males						Females					
	Cases		Controls		Odds ratio	95% CI*	Cases		Controls		Odds ratio	95% CI*
	No	(%)	No.	(%)			No	(%)	No	(%)		
Exposure in childhood												
No	15	(38)	41	(35)	1.00†		22	(32)	81	(43)	1.00†	
Yes	25	(62)	76	(65)	0.90	0.43–1.89	47	(68)	106	(57)	1.55	0.95–2.79
No. of smokers in household in childhood												
0	15	(38)	41	(35)	1.00†		22	(32)	81	(44)	1.00†	
1	18	(45)	53	(46)	1.12	0.46–2.70	39	(57)	82	(44)	1.75	0.91–3.35
2+	7	(17)	22	(19)	1.13	0.34–3.75	8	(11)	23	(12)	1.27	0.43–3.78
Exposure in adulthood at home												
No	28	(68)	83	(71)	1.00†		26	(38)	68	(36)	1.00†	
Yes	13	(32)	34	(29)	1.13	0.53–2.45	43	(62)	119	(64)	0.95	0.53–1.67
No. of smokers in household in adulthood												
0	28	(68)	83	(72)	1.00†		26	(38)	68	(37)	1.00†	
1	6	(15)	28	(24)	0.64	0.19–2.13	34	(49)	93	(50)	0.96	0.50–1.84
2+	7	(17)	5	(4)	4.15	1.34–12.87	9	(13)	25	(13)	0.94	0.34–2.63
Exposure at work‡												
No	18	(44)	52	(44)	1.00†		23	(40)	64	(43)	1.00†	
Yes	23	(56)	65	(56)	1.02	0.50–2.09	35	(60)	85	(57)	1.15	0.62–2.13
Exposure in cars												
No	32	(78)	99	(85)	1.00†		50	(72)	155	(83)	1.00†	
Yes	9	(22)	18	(15)	1.55	0.63–3.78	19	(28)	32	(17)	1.84	0.96–3.53
Exposure in trains, buses, and other transportation												
No	41	(100)	112	(96)	1.00†		62	(90)	183	(98)	1.00†	
Yes	0	(0)	5	(4)	0.27	0.01–13.99	7	(10)	4	(2)	5.17	1.46–18.24
Exposure in social situations												
No	16	(39)	55	(47)	1.00†		41	(59)	120	(64)	1.00†	
Yes	25	(61)	62	(53)	1.39	0.67–2.86	28	(41)	67	(36)	1.22	0.69–2.15

* CI, confidence interval.

† Referent group.

‡ For females, this category excludes housewives

Between 1985 and 1990, subjects were asked about history of previous respiratory disease, including chronic bronchitis, emphysema, asthma, and tuberculosis. None of the cases and less than 4 percent of controls reported a history of either chronic bronchitis or emphysema.

DISCUSSION

Epidemiologic studies of exposure to environmental tobacco smoke in relation to lung cancer and other chronic diseases that occur late in life are beset by a number of methodological problems that need to be kept in mind when interpreting their results. These problems include: misclassification of current or past smokers as never smokers; misclassification of environmental tobacco smoke exposure; selection bias; confirmation of primary lung cancer and histology; data collection methods (use of surrogates; telephone/mailed interviews); and potential confounding. In addition, it should be noted that because there is no

standard set of questions for assessment of environmental tobacco smoke, the type and extent of the information collected, as well as the exposure variables created, differ from study to study.

The present study differs from a number of previous studies in several respects. First, newly diagnosed cases of lung cancer were interviewed in collaborating hospitals at the time of initial diagnosis. In many instances, the case was interviewed based on a clinical diagnosis and only later was confirmed when pathology results became available. Because there was no interval between diagnosis and interview, cases were not lost due to mortality. In addition, the refusal rate in this study was low (<10 percent), minimizing the possibility of selection bias.

Second, all interviews were conducted with the subjects themselves, in contrast to studies in which surrogates were used. Use of proxy respondents could lead to biased assessment of exposure, as suggested by one study that tabulated the odds ratio for lung cancer

TABLE 3. Measures of environmental tobacco smoke exposure among lifetime nonsmoker lung cancer cases and controls in a US hospital case-control study, 1983–1990*

Variable	Males				Females			
	Cases		Controls		Cases		Controls	
	Mean	(SD)	Mean	(SD)	Mean	(SD)	Mean	(SD)
No. of smokers in childhood	1.4	(0.7)	1.3	(0.6)	1.2	(0.4)	1.2	(0.5)
Duration of childhood exposure (years)	20.5	(8.1)	19.9	(9.7)	19.8	(7.7)	19.3	(8.2)
Duration of adulthood exposure (years)	22.8	(15.7)	15.6	(14.2)	26.2	(13.0)	23.0	(13.7)
Duration of spousal exposure (years)	23.6	(16.5)	18.1	(13.3)	26.4	(12.0)	24.4	(11.9)
No. of cigarettes smoked by spouse (weighted average)	10.9	(9.3)	7.4	(8.8)	13.6	(9.6)	14.1	(14.4)
Duration of work exposure (years)	28.5	(11.5)	29.6	(13.5)	22.1	(11.5)	22.3	(12.5)
Duration of exposure in social situations (years)	23.3	(14.8)	22.2	(11.9)	23.6	(12.6)	24.6	(15.2)

* Means (standard deviations (SD)) are based on the number of subjects who reported a particular exposure

in nonsmoking women with their husband's smoking habits as reported by different types of respondents (5). Third, the questionnaire was designed to characterize each exposure source as fully as possible, in order to include all important sources of exposure, as well as, where possible, to obtain more than one indicator of a particular exposure. The questionnaire included information on multiple spouses, roommates, and other household members. For each smoker in the household in adulthood, information was obtained on number of cigarettes per day, hours per day of exposure, and a subjective rating of exposure. In addition, subjects whose spouses smoked were asked whether the spouse smoked in the bedroom.

We examined the agreement between different items in the questionnaire relative to a common exposure. For example, among female controls, wives who reported that their husband smoked in the bedroom reported that he smoked a mean of 20 cigarettes per day in her presence in contrast to women whose husbands smoked but not in the bedroom, for whom a mean of 11 cigarettes per day was reported. Among male controls, the corresponding means were 16 cigarettes per day compared with 5 cigarettes per day. Smoking in the bedroom may be indicative of heavy exposure to spousal smoking. For female controls, rating their exposure to their husband's smoke as "light," "moderate," or "heavy," the mean numbers of cigarettes reported smoked by the husband were 6, 13, and 26, respectively. For male controls who reported different intensities of exposure to a wife's smoke, the corresponding mean numbers of cigarettes smoked were 4, 8, and 14. Similar trends were seen among cases. This consistency between different independent measures of exposure increases confidence in the va-

lidity of these data. In addition, the prevalence and duration of exposure in childhood is similar between males and females, whereas, in adulthood, exposure at home is consistently greater (whether measured by prevalence or amount smoked by the spouse) in females compared with males. This pattern is in agreement with previous findings (6).

Reproducibility of responses on environmental tobacco smoke exposure was evaluated for 48 subjects (cases and controls) who were reinterviewed by telephone 1–2 months following the original interview. The Kappas for specific questions regarding exposure before age 21 years were as follows: mother's smoking (yes/no), 0.90; father's smoking (yes/no), 0.72; other's smoking (yes/no), 0.73; and any exposure (yes/no), 0.72. For exposure after age 21 years (yes/no), Kappa = 0.63. For exposure to spousal smoking (yes/no), Kappa = 0.72. These values are similar to those reported in previous studies (7, 8). Reproducibility of quantitative items, such as number of cigarettes smoked by the spouse or number of hours per day of exposure to environmental tobacco smoke, is generally much poorer.

The present study had limited statistical power to detect an effect of exposure to environmental tobacco smoke. In females, the power to detect a significant association with having a husband who smoked (60 percent prevalence in the controls), with 2-tailed $\alpha = 0.05$, was 83 percent for detecting an odds ratio of 2.50, 61 percent for an odds ratio of 2.00, and 27 percent for an odds ratio of 1.50. The power to detect an association given a 30 percent prevalence of exposure among the controls (lowest tertile of smoker-years) was 89 percent for detecting an odds ratio of

TABLE 4. Association of spousal smoking with lung cancer in lifetime nonsmokers in a US hospital case-control study, 1983–1990*

Variable	No. of cases	No. of controls	Odds ratio†	95% confidence interval
<i>Males</i>				
Spouse smokes				
No	28	79	1.00‡	
Yes	11§	19	1.60	0.67–3.82
Amount smoked by spouse(s)¶				
None	28	79	1.00‡	
1–10 cigarettes/day	5	17	0.74	0.24–2.23
11+ cigarettes/day	5	2	7.48	1.35–41.36
Spouse smokes in bedroom				
No	6	14	1.00‡	
Yes	5	5	5.02	0.72–35.01
Spouse smokes in bedroom				
No/nonsmoker	34	93	1.00‡	
Yes	5	5	2.67	0.72–9.85
<i>Females</i>				
Spouse smokes				
No	26	71	1.00‡	
Yes	41	102	1.08	0.60–1.94
Cigarettes only	30	78	0.98	0.55–1.73
Pipes/cigars only	5	13	0.98	0.33–2.92
Cigarettes + pipes/cigars	6	11	1.44	0.51–4.11
Amount smoked by spouse(s)¶				
None	26	71	1.00‡	
1–10 cigarettes/day	17	50	0.82	0.42–1.61
11+ cigarettes/day	12	28	1.06	0.49–2.30
Spouse smokes in bedroom				
No	28	70	1.00‡	
Yes	13	32	1.09	0.49–2.42
Spouse smokes in bedroom				
No/nonsmoker	54	141	1.00‡	
Yes	13	32	1.07	0.52–2.19

* Limited to those who were ever married.

† Adjusted for age and years of education (as continuous variables) and type of hospital (cancer center vs. other).

‡ Referent group.

§ Includes 1 cigar/pipe smoker.

¶ Referent group has no exposure in adulthood at home; exposure status based on weighted average number of cigarettes per day smoked by spouse(s) throughout marriage(s).

2.50, 67 percent for an odds ratio of 2.00, and 29 percent for an odds ratio of 1.50.

Given the limited power, we were particularly interested in looking for consistency between different measures of exposure and for evidence of an elevated odds ratio in subgroups hypothesized a priori to have high exposure. Thus, we would a priori expect to see evidence of an increased risk in women with husbands who smoked rather than in men with wives who smoked, in women whose husbands were heavier smokers (as indicated by number of cigarettes smoked per day or by whether the husband smoked in the bedroom), and in women who characterized their smoke exposure due to their husband as "heavy." No such associations were observed.

We were not able to gain access to pathology slides for an independent review of the histology; however, the distribution of cell types in this study is similar to that in studies in which histology was independently evaluated, when allowance is made for the higher proportion of other/mixed cell types (9, 10). Fifty-seven percent of the cases in the present study came from a single cancer center (Memorial Sloan-Kettering Cancer Center). To the extent that some cases of metastasis to the lung may have been incorrectly classified as primary lung cancer, this would tend to obscure a true association with environmental tobacco smoke, if one exists.

Nonsmoking status of the subjects was not validated in this study (i.e., by urinary cotinine measurement,

TABLE 5. Association of smoker-years in childhood and adulthood and at work with lung cancer in lifetime nonsmokers in a US hospital case-control study, 1983–1990

Smoker-years/ job-years	Males		Females	
	Odds ratio†	95% CI‡	Odds ratio†	95% CI‡
In childhood				
Low	1.00§		1.00§	
Intermediate	0.95	0.38–2.42	1.73	0.84–3.58
High	1.39	0.57–3.39	2.19*	1.06–4.50
In adulthood				
Low	1.00§		1.00§	
Intermediate	1.98	0.65–6.02	1.30	0.65–2.63
High	1.50	0.46–4.89	1.14	0.56–2.33
At work				
Low	1.00§		1.00§	
Intermediate	1.13	0.44–2.90	0.94	0.42–2.10
High	1.21	0.47–3.13	1.35	0.64–2.84

* *p* value for test for linear trend = 0.02.

† Adjusted for age and years of education (as continuous variables) and type of hospital (cancer center vs. other).

‡ CI, confidence interval

§ Referent group

which is reflective of smoking in the past few days). However, the absence of any prior history of chronic bronchitis or emphysema among cases enrolled from 1985 to 1990 provides indirect support for their being nonsmokers. (For lung cancer among women who had ever smoked, the prevalence of chronic bronchitis in our study was 11 percent and that of emphysema was 8 percent.)

In surveying existing epidemiologic studies of environmental tobacco smoke and lung cancer in nonsmokers, several areas of inconsistency should be noted. First, while several large studies carried out in the United States show a significant association with spousal smoking (9, 11), one study (10) reported a borderline elevated odds ratio for the highest level of cumulative exposure only (odds ratio for >40 pack-years exposure from all household members = 1.3, 95 percent CI 1.0–1.7). Other studies, including those by Janerich et al. (12) and the present study, show no evidence of an association with spousal smoking.

Second, different studies show an association of spousal smoking with different cell types. The largest study (9) showed a significant association with adenocarcinoma and a borderline association with all other histologic types; others noted an association only with squamous/small cell carcinoma (13, 14); two studies showed stronger associations with squamous cell carcinoma (or all types other than adenocarcinoma) than with adenocarcinoma (5, 11), and one study reported an association only for "other/mixed" cell types, of which the numbers were small (10).

Third, several studies indicate an association of environmental tobacco smoke exposure in childhood

with lung cancer (11, 12), whereas others offer no support for an association (9, 10). Inconsistency of results regarding exposure in childhood is not surprising, given the difficulty of obtaining reliable information, particularly from surrogate respondents.

While an association between exposure to environmental tobacco smoke and lung cancer in never smokers has compelling biological plausibility and potentially important public health implications (1, 15), the methodological difficulties confronting these studies and the inconsistencies in their results illustrate the difficulty in using epidemiologic methods to establish and verify small excess risks.

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